

of the plasma cells was confirmed by staining with Unna and Pappenheim's methyl-green and pyronine. It is to be noted that this tumour bears no relationship to the myeloid epulis or osteoclastoma.

The diagnosis of solitary myeloma having been established, the patient was referred for x-ray therapy to Dr. Phillip Flood, to whom we are indebted for co-operation with this treatment and for furnishing notes on the clinical progress of the case.

**Conclusion**

The myeloma is a true malignant neoplasm, which in this case proved responsible for the pain which had at first been attributed to simple toothache. Several theories have been advanced regarding the aetiology of these tumours. Trauma and chronic osteitis may have an influence on the malignant transformation of cells of the bone marrow. In the present case the histology reveals that an osteitic process can be traced in the tumour region. Such a deviation from the normal may have contributed to the formation of the growth. A thorough radiological examination did not reveal any metastatic tumours. The treatment of choice for plasmacytomata in this region is surgical removal followed by x-ray therapy (Gootnick, 1945).

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**SIGNIFICANCE OF THE GRAM TEST FOR BACTERIA IN RELATION TO PENICILLIN BACTERIOSTASIS**

BY

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We have already shown that nucleic acids possess the property of antagonizing the inhibitory action of penicillin on susceptible pathogens and that they can also reverse such actions (Pandalai and George, 1947a, 1947b). Further, nucleic acids restored original characteristics to bacterial cells which had undergone changes in morphology and Gram-staining reaction due to contact with penicillin. We also demonstrated that nucleic acids failed to have any of these effects on Gram-negative bacteria, such as *Bacterium coli*, normally insensitive to penicillin, but which, however, were inhibited by higher concentrations (George and Pandalai, 1947).

It is now known that some other antibiotics are Gram-sensitive. It has also been demonstrated (Henry and Stacey, 1943, 1946) that the staining quality characteristic of the Gram-positive organism is associated with the presence of magnesium ribonucleate within the organism, and that this substance prepared from commercial sources was capable of restoring the Gram-positive quality to bacteria from which it had been removed by 2% bile salt in normal saline.

We have studied the influence of added magnesium ribonucleate on the growth of Gram-negative organisms kept in contact with penicillin. It might be expected that in the presence of added magnesium ribonucleate the Gram-negative organisms which are ordinarily insensitive to

penicillin would in their life processes be more in agreement with the sensitive organisms, and consequently would be inhibited by lower concentrations of the drug. It was actually found that magnesium ribonucleate stood to the Gram-negative organisms in just the same relation that nucleic acid stood to the Gram-positive organisms, in that it antagonized the inhibitory action of penicillin and also allowed the organisms to grow from a non-viable condition produced by contact with penicillin. The results are given in Tables I and II.

TABLE I.—Showing the Influence of Magnesium Ribonucleate on the Penicillin Inhibition of *Bact. coli*

Penicillin Alone (Units per ml.)	Magnesium Ribonucleate Alone	Magnesium Ribonucleate and Penicillin	Broth Control
12.0 +	1/2,500 +++	1/2,500 { 12.0 ++ 15.0 ++ 17.5 ++	
15.0 -	1/5,000 +++	1/5,000 { 12.0 ++ 15.0 ++ 17.5 +	+++
17.5 -	1/10,000 +++	1/10,000 { 12.0 ++ 15.0 + 17.5 +	

- indicates complete inhibition; + indicates growth; ++ fairly good growth; +++ very good growth.

TABLE II.—Showing the Reversibility of Penicillin Action on *Bact. coli* produced by added Magnesium Ribonucleate

Penicillin (Units per ml.)	Magnesium Ribonucleate Added			Broth Control
	After 3 Hours	After 6 Hours	After 24 Hours	
12.0 +	++	++	++	
15.0 -	++	++	++	
17.5 -	++	++	++	
20.0 -	++	++	++	+++

The magnesium ribonucleate used was a neutral solution of the magnesium salt of pure yeast nucleic acid, and *Bact. coli* was the test organism. The results show, however, that the addition of magnesium ribonucleate to *Bact. coli* cultures does not help the organisms to become susceptible to lower concentrations of penicillin. This means that magnesium ribonucleate alone cannot convert the Gram-negative organism into a Gram-positive one, at any rate from the point of view of susceptibility to penicillin action. Even, granting that magnesium ribonucleate has some far-reaching effects on an organism (Stacey, 1947) in its relation to the Gram test, it cannot be said to possess any special influence on the specificity of the inhibitory action of penicillin, as the susceptibility of certain organisms, such as *Streptococcus faecalis*, the gonococci, and the meningococci, will still remain unexplained.

That the magnesium ions, quite apart from the ribonucleate moiety, in the magnesium ribonucleate exert a pronounced influence on the growth of *Bact. coli* in contact with penicillin is seen from the results given in Table III.

TABLE III.—Showing the Influence of Magnesium Ions on the Growth of *Bact. coli* in the Presence and Absence of Penicillin

Penicillin Alone (Units per ml.)	Mg ++ Added as MgSO <sub>4</sub> Solution Alone	MgSO <sub>4</sub> and Penicillin	Broth Control
6.0 ++	0.1% +++	0.1% { 6 ++ 8 ± 10 - 12 - 15 -	+++
8.0 ++			
10.0 ++			
12.0 +			
15.0 -	0.2% +++	0.2% { 6 ++ 8 ± 10 - 12 - 15 -	+++
17.5 -			

The minimum inhibiting concentration of penicillin for *Bact. coli* diminishes to about 50% of its original value when magnesium ions are present in the culture treated with penicillin. It is interesting to note that exactly the same type of results was obtained with a strain of *Shigella dysenteriae*. It would thus seem that magnesium ions have the interesting property of converting normally insensitive organisms to a state more closely resembling that of the sensitive pathogens, probably by altering their metabolic reaction pathways. It is thus obvious that there is need for further work to assess the actual significance of (1) the Gram reaction in its relation to sensitivity or otherwise of the respective pathogens to penicillin, and (2) the assumption (Haslett, 1947) that the ability to produce penicillinase may be tied up with the absence of magnesium ribonucleate from penicillin-resistant organisms. Work on these aspects is in progress.

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## LUGOL'S SOLUTION IN FAILING LACTATION

BY

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The capacity for satisfactory lactation shown by individual women depends on the quantity of breast tissue available and its degree of differentiation. It is unlikely that hormone therapy can significantly alter the quantity of tissue available, but it may influence a poor breast temporarily to secrete more milk. Dried thyroid gland may increase the rate of milk production since it raises the basal metabolic rate, and there is experimental evidence that this increase in milk output may amount to as much as 20–30% of the daily output. This effect is only temporary, and ceases when the hormone is omitted (Engel, 1947; Folley, 1947).

Partial or total failure of breast-feeding is common. Robinson (1943, 1947a, 1947b, 1947c) has described the results of hormone therapy in women whose lactation is judged likely to fail. As a result of this work it was concluded that dried thyroid gland caused a greater increase in milk yield than any other hormone. In view of this finding Lugol's solution of iodine was tried, and was found to be even more successful. It is difficult to explain why this should be so, for it is known that thyroid extracts and iodine have opposite effects upon the abnormal B.M.R.

Robinson (1943) test-weighed the infant on the fifth day, and if the milk output was less than 10 oz. (284 ml.) it was considered likely that lactation might fail. In a consecutive series of 99 such instances where lactation was judged to be failing test-weighing was done daily until discharge and again at the fourth week. Of these women 72 were treated as controls and the remaining 27 were given six drops of Lugol's solution in milk twice a day. (Lugol's solution: 5%

iodine in 10% aqueous potassium iodide.) This treatment was started on the sixth day and continued until discharge or until the output reached 16 oz. (454 ml.). Lugol's solution appeared to increase the milk output.

This work has been repeated in the present series using exactly the same indication of failure to establish lactation and the same dose of Lugol's solution. Test-weighing was done on the fifth day, and if the output was less than 10 oz. the case was admitted to the experimental series. Alternate cases were used as controls or given Lugol's solution as indicated. Unfortunately, routine test-weighing proved impossible after discharge, which was usually on the twelfth day after delivery. Concurrently all infants in hospital were test-weighed on the fifth and tenth days to provide an indication of normality. One serious difficulty was encountered in making the work strictly comparable, since in this maternity unit the technique of Waller (1937, 1947) is used both to encourage lactation and to avoid congestion. This involves antenatal and postnatal expression of the colostrum and milk and the administration of moderate doses of stilboestrol in the early phase of congestion. However, it was decided to use the milk output, as measured by test-weighing, as the indication of failure to establish lactation, but to record the total output (test-weigh and expressed milk) in the results. By this means it has been possible to estimate the effect of the iodine solution on total milk output whilst adhering to the criteria of Robinson; furthermore, in this way it is possible to ignore the sucking power of the infant.

Part of Waller's technique is to give stilboestrol early in breast congestion. Since it was considered possible that this might affect lactation adversely patients who had received stilboestrol were excluded from the trial series. Nevertheless test-weighing was done, and the results are recorded in the Table. In this particular group there were

## Results of Tests

Group	No.	5th Day Output Bulk (oz.)	5th Day Mean (oz.)	10th Day Output Bulk (oz.)	10th Day Mean (oz.)
Normal at 5th day	151	2,330 (66.2 l.)	15.4 (436 ml.)	3,019 (85.77 l.)	19.9 (565 ml.)
Normal at 5th day. Stilboestrol given	11	190 (5.4 l.)	17.2 (490 ml.)	221 (6.28 l.)	20.0 (568 ml.)
Failed at 5th day. Stilboestrol given	43	238 (6.76 l.)	5.5 (156 ml.)	653 (18.5 l.)	15.2 (432 ml.)
Failed at 5th day. Controls	24	199 (5.65 l.)	8.3 (235 ml.)	362 (10.28 l.)	15.0 (425 ml.)
Failed at 5th day. Iodine given	19	167 (4.74 l.)	8.5 (240 ml.)	262 (7.44 l.)	13.7 (390 ml.)

54 cases. On the fifth day eleven had an output over 10 oz. and 43 an output less than 10 oz. This second group of possible failures who had received stilboestrol were not given Lugol's solution. The results in these two groups appear to indicate that stilboestrol does not adversely affect lactation itself, and since it diminishes engorgement and the tendency to abscess formation it seems reasonable to continue using it in moderate dosage, provided that it has no harmful effects on the female reproductive system as a whole.

It will be seen from the above results that Lugol's solution appeared to have no influence upon lactation, at least not a beneficial one. This is at variance with the findings of Robinson and would seem to nullify her conclusions that iodine increased the milk output and that failing lactation depended upon a deficiency of iodine intake. On the other hand, so far as these figures go it can be seen that stilboestrol given in the first few days of lactation has no permanent deleterious effect upon the milk output. It was considered unnecessary to append the statistical material from this work, since it did not clarify the results.